

**What is Claimed:**

1. A method of identifying compounds that modulate mammalian histamine H4 receptor activity, comprising:
  - a) combining a putative modulator compound of mammalian histamine H4 receptor activity with mammalian histamine H4 receptor and a known histamine receptor H4 ligand; and
  - b) measuring an effect of the modulator on the protein function or its ability to bind the ligand, wherein said effect is a modulation selected from the group consisting of inhibition, activation, antagonist, agonist, and inverse agonist activity,wherein said modulator compound is a modulator of mast cell chemotaxis or basophil chemotaxis.
2. The method of claim 1, wherein the effect measured in step b) is inhibition by competition between the modulator of step a) and a known histamine receptor H4 ligand for binding to the receptor.
3. The method of claim 1, wherein the effect measured in step b) is modulation of a histamine H4 receptor intracellular second messenger.
4. The method of claim 3, wherein the intracellular second messenger is selected from the group consisting of cAMP, calcium, and a reporter gene product.
5. The method of claim 1, wherein said compound is a modulator of mast cell chemotaxis.
6. The method of claim 1, wherein said compound is a modulator of basophil chemotaxis.
7. A compound identified using the method of claim 1, wherein said compound is an inhibitor of a mammalian histamine H4 receptor function and an inhibitor of mast cell chemotaxis or basophil chemotaxis *in vivo* or *in vitro*.
8. A compound identified using the method of claim 1, wherein said compound is an agonist, antagonist, or inverse agonist of a mammalian histamine H4 receptor.

9. A compound identified using the method of claim 1, wherein said compound modulates expression of a gene encoding the mammalian histamine H4 receptor.
10. A monospecific antibody immunologically reactive with a mammalian histamine H4 receptor protein, wherein said antibody modulates mast cell chemotaxis or basophil chemotaxis.
11. The antibody of claim 10, wherein the antibody blocks histamine binding or activation of the mammalian histamine H4 receptor protein.
12. A pharmaceutical composition comprising a compound active in the method of claim 1 and a pharmaceutically acceptable carrier wherein said compound is a modulator of asthma or allergic responses.
13. A method of treating a patient in need of such treatment to modulate asthma or allergic responses or a disease or condition that is mediated by asthma or allergic responses and histamine H4 receptor comprising administration of the pharmaceutical composition of claim 12.
14. A pharmaceutical composition comprising a compound active in the method of claim 1 and a pharmaceutically acceptable carrier wherein said compound is a modulator of mast cell chemotaxis.
15. A method of treating a patient in need of such treatment to modulate asthma or allergic responses or a disease or condition that is mediated by mast cell chemotaxis and histamine H4 receptor comprising administration of the pharmaceutical composition of claim 14.
16. A pharmaceutical composition comprising a compound active in the method of claim 1 and a pharmaceutically acceptable carrier wherein said compound is a modulator of basophil chemotaxis.

17. A method of treating a patient in need of such treatment to modulate asthma or allergic responses or a disease or condition that is mediated by basophil chemotaxis and histamine H4 receptor comprising administration of the pharmaceutical composition of claim 16.
18. A pharmaceutical composition comprising a compound that modulates mammalian histamine H4 receptor activity and a pharmaceutically acceptable carrier, wherein said compound is a modulator of mast cell or basophil chemotaxis *in vitro* or *in vivo*.
19. The pharmaceutical composition of claim 18, wherein the compound inhibits mast cell chemotaxis.
20. The pharmaceutical composition of claim 18, wherein the compound inhibits basophil chemotaxis.
21. The pharmaceutical composition of claim 18, wherein the compound is an agonist, antagonist, or inverse agonist of a mammalian histamine H4 receptor.
22. The pharmaceutical composition of claim 18, wherein the compound modulates expression of a gene encoding the mammalian histamine H4 receptor.
23. The pharmaceutical composition of claim 18, wherein the compound further modulates eosinophil shape change *in vitro* or *in vivo*.
24. A method of treating a patient in need of such treatment to modulate asthma or allergic responses or a disease or condition that is mediated by mast cell or basophil chemotaxis and histamine H4 receptor comprising administering a pharmaceutical composition comprising a compound that modulates mammalian histamine H4 receptor activity and a pharmaceutically acceptable carrier, wherein said compound is a modulator of mast cell or basophil chemotaxis *in vitro* or *in vivo*.
25. The method of claim 24, wherein the pharmaceutical composition comprises a compound that inhibits mast cell chemotaxis.

26. The method of claim 24, wherein the pharmaceutical composition comprises a compound that inhibits basophil chemotaxis.
27. The method of claim 24, wherein the pharmaceutical composition comprises a compound that is an agonist, antagonist, or inverse agonist of a mammalian histamine H4 receptor.
28. The method of claim 24, wherein the pharmaceutical composition comprises a compound that modulates expression of a gene encoding the mammalian histamine H4 receptor.
29. The method of claim 24, wherein the pharmaceutical composition comprises a compound that modulates eosinophil shape change *in vitro* or *in vivo*.
30. A method of identifying compounds that modulate mammalian histamine H4 receptor-mediated chemotaxis of mast cells to histamine, the method comprising:
  - a) in the presence or absence of a test compound being tested as a histamine H4 receptor modulator, placing mast cells in proximity to histamine under conditions enabling movement of the mast cells toward the histamine; and
  - b) measuring an effect of the histamine H4 receptor modulator on the movement of the mast cells toward the histamine, wherein an increase or decrease in rate of mast cell movement toward the histamine or in number of mast cells that move toward the histamine is indicative that the test compound modulates histamine H4 receptor-mediated chemotaxis of the mast cells to histamine.
31. A method of determining if a histamine H4 receptor modulator modulates sub-epithelial accumulation of mast cells in a mammalian trachea in response to exposure to histamine or an allergen, the method comprising:
  - a) in the presence or absence of pre-treatment with a histamine H4 receptor modulator, exposing a mammal to an aerosol comprising histamine or an allergen under a regimen that would, in the absence of the modulator, result in a pre-determined amount of sub-epithelial mast cell accumulation in the mammal's trachea; and
  - b) comparing sub-epithelial mast cell accumulation in the mammal's trachea in the presence and absence of the histamine H4 receptor modulator, a change in the sub-epithelial mast cell accumulation in the presence of the modulator as

compared to in the absence of the modulator being indicative that the histamine H4 receptor modulator modulates the sub-epithelial accumulation of mast cells in the mammal's trachea in response to the exposure to histamine or an allergen.